Claim 29, line 3, replace "the" with --a--.

Claim 33, line 5, before "subfamily" insert --(pleomorphic adenoma gene 1)--.

Claim 33, line 6, replace "CNNB1" with --CTNNB1 (β-catenin)--.

Claim 47, line 3, after "PLAG1" insert --(pleomorphic adenoma gene 1)--.

REMARKS

Claims 28, 29, 33 and 47 have been amended. Claims 28, 29, 32-34 (a)-(d), 35 and 47 remain in the application. Reexamination and allowance of the amended claims are requested.

The Examiner has objected to the specification and Figures because they contain sequences that are not identified by SEQ ID NO. The addition of SEQ ID NOs to the present specification and Figures will be made in due course in the prosecution of this patent application.

The Examiner has rejected claims 28, 29, 32, 33, 34 (a) - (d), 35 and 47 under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, for purported lack of utility. The Examiner asserts that the specification fails to disclose a specific asserted utility for the claimed isolated nucleic acid or for the oligonucleotide or polynucleotide as probes and primers. The Examiner also asserts that no direct connection is made between the claimed PLAG1 gene and a specific tumor disease, and the functionality of the nucleic acid and protein as subjected to insertions, deletions, and substitutions is not demonstrated. However, it is believed that this rejection is not appropriate under the Revised Interim Utility Guidelines issued by the United States Patent and Trademark Office. Under the Utility Guidelines a utility, if not readily apparent (i.e., well-established) must be described specifically in the specification and the utility must be substantial and credible. It is believed that substantial, credible utilities, as defined in the Utility Guidelines, are provided. Specifically, it is believed that the use of the claimed nucleic acids to identify pleomorphic

adenomas and the like is not only a credible utility, but specific and substantial. The identification of the chromosome 8q12 breakpoint and the direct chromosome walking from this breakpoint, leading to identification of the rearranged genes strongly supports the asserted utility of the claimed nucleic acids as probes and primers for identifying the specified proliferative diseases. Also, the Examiner lists a number of specific uses for the probes of the present invention as diagnostic markers on page 8 of the Office Action under the heading "*III. Presence and Absence of Working Examples.*" In addition, PLAG1, which is not normally expressed in adult tissues but in embryonic tissues, is over-expressed in benign salivary gland tumors (by promoter swapping with CTNNB1). Consequently, observation of the expression of PLAG1 is a diagnostic tool in the differentiation of benign and malignant tumors (see page 50 and Example 5 of the specification). Furthermore, suppression of PLAG1 can be used in anti-tumor therapy (see Example 12 at page 64 of the specification). For these reasons, it is believed that the utility of the present invention has been demonstrated.

The Examiner has rejected claims 28, 29, 32, 33, 34 (a)-(d), 35 and 47 under 35 U.S.C. § 112, first paragraph, for purported lack of written description and for purported lack of enablement for "at least part of the PLAG1 gene" and "degenerate sequences thereof." With regard to enabling "parts of the PLAG1 gene," pages 47 and 48 and Figure 4 of the specification refer to different regions and fragments (zinc fingers, nuclear localization signals, serine-rich carboxy-terminal part, activation domains interacting with other proteins) of PLAG1. Therefore, the nucleotide sequences and amino acid sequences of PLAG1 and parts thereof are explicitly enabled in the specification. It is therefore believed that the person skilled in the art, reading the specification and Examples 1 to 12, will be able to repeat and use the invention. Furthermore, at page 7, line 1 of the current Office Action, the Examiner states that the present invention makes use of classical molecular biological

techniques that are well known in the prior art. Once the sequence of a new gene and specific regions or fragments therein have been characterized, it would be obvious to use classical molecular biological techniques to make use of parts of the new gene. With regard to enabling "degenerate sequences thereof," techniques for the degeneration of the genetic code have been known for a long time in the art, so that it is not necessary to provide explicit information in the specification on how to make degenerate sequences of the fully disclosed nucleic acid sequence of the present invention. Therefore, it is believed that the claims, which refer to part of the PLAG1 gene or sequences complementary thereto, are enabled by the specification and by what is known to the person skilled in the art.

The Examiner has rejected claims 28 and 29 under 35 U.S.C. § 112, second paragraph, for purported indefiniteness. The Examiner asserts that claims 28 and 29 lack the proper antecedent basis for "the complementary strand thereof". The claims have been amended to refer to "a complementary strand thereof".

The Examiner has rejected claims 28, 29, 33, 34 (a)-(d), 35 and 47 under 35 U.S.C. § 112, second paragraph for purported indefiniteness. The Examiner asserts that the abbreviations "PLAG" and "PLAG1" in claim 47 may have more than one meaning. Claim 47 has been amended to recite the full name of the gene.

The Examiner has rejected claims 33 and 34 under 35 U.S.C. § 112, second paragraph for purported indefiniteness. The Examiner asserts that the abbreviation "CNNB1" may have more than one meaning, and is not used in the specification. Claim 33 has been amended to recite the full name of the gene.

The Examiner has rejected claims 47 and 33 under 35 U.S.C. § 102 (b) for purported anticipation by Kraus et al. (Genomics, 23, pages 272-274, December 1994). The Examiner asserts that Kraus discloses an isolated nucleotide sequence wherein the nucleic acid is an oligonucleotide and a polynucleotide fragment having a sequence of at least a part

of a gene of the PLAG1 subfamily. The Examiner also asserts that Kraus discloses a nucleic acid having a nucleotide sequence of at least a part of a T-gene selected from the group consisting of the PLAG1 subfamily of zinc finger protein genes, the CTNNB1 gene and fusion protein, or complementary degenerate versions of the nucleotide sequence. However, the inventors have performed a BLAST (Basic Local Alignment Search Tool) search on the nucleotide and amino acid level and did not find any significant similarity between the PLAG1 of the invention (7313 bp) and CTNNB1 in Kraus et al. (See Annex 3). Therefore it is believed that the nucleic acid of Kraus et al. does not anticipate the nucleic acid of the present invention.

The Examiner has rejected claims 28 and 29 under 35 U.S.C. § 102 (a) for purported anticipation by Kas et al. (July 24, 1996) Gene Bank Accession No. U65002, Lab for Molecular Oncology, CAS Registry No. 186288-05-1. The Examiner asserts that Kas et al. discloses an isolated nucleic acid comprising a nucleotide sequence identical to the zinc finger domains of the PLAG1 nucleotide sequence in Figure 4A of the present application, and an isolated nucleic acid comprising a nucleotide sequence identical to the nucleotide sequence of the PLAG1 gene depicted in Figure 4A. Kas et al. have submitted the sequence of the present invention as a "Direct Submission." However, Kas et al. have requested, as is common practice and is provided for by the regulations of the Genbank (see Annex 1), to keep this entry confidential until the publication of the corresponding article. As is shown in the in the annexed (Annex 2) NCBI Sequence revision history, the article was not published before February 12, 1997. The publication date of the corresponding *Nature Genetics* article is February 15, 1997. Therefore the article was not made public before the August 22, 1996 priority date of the present application. Also submitted is a Declaration signed by the Assignee explaining why the Kas et al. Publication , which is the inventors' own work, has an author list different from the inventorship of the above-identified patent application.

The Examiner has rejected claims 47, 32, 33, 34 (a)–(d), and 35 under 35 U.S.C. § 102(a) for purported anticipation by Nollet et al. (*Genomics*, March 1996). The Examiner asserts that Nollet et al. discloses a nucleic acid in isolated form wherein the nucleic acid is an oligonucleotide and a polynucleotide fragment having a sequence having at least a part of a gene in the PLAG1 gene subfamily. However, the inventors have performed a BLAST (Basic Local Alignment Search Tool) search on the nucleotide and amino acid level and did not find any significant similarity between the PLAG1 of the invention (7313 bp) and CTNNB1 in Nollet et al. (3362 bp). Therefore it is believed that the nucleic acid of Nollet et al. does not anticipate the nucleic acid of the present invention.

In view of the above amendments and remarks, it is believed that the claims are in condition for allowance. Reconsideration of the rejections is requested. Allowance of claims 28, 29, 32-34 (a)-(d), 35 and 47 is respectfully requested.

Respectfully submitted,

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